59. (new) The SIV packaging vector of claim 55, wherein the vector comprises the nucleic acid sequence shown in SEQ ID NO: 11.

Remarks

Claims 7-17, 21 and 43-46 were pending. Due to the restriction requirement, claim 16 is cancelled without prejudice to prosecution in a future application. Claim 10 was cancelled as duplicative of claim 8. Claims 47-59 are added. Therefore, claims 7-9, 11-15, 17, 21 and 43-59 are now pending.

Telephone Interview

Applicant thanks Examiner Hill and his supervisor James Housel for a telephone interview with Applicant's representative Sheree Lynn Rybak, Ph.D. on March 29, 2005. During this interview, all of the claim rejections were discussed. Provided below is a summary of the conversation, and agreements that were reached.

Applicant agreed to amend claim 10 and 15 to address the claim objections.

With regard to the 35 U.S.C. § 112, second paragraph rejections of claim 7, it was agreed that amending the phrase "A packaging vector derived from HIV-2" to "An HIV-2 packaging vector" would overcome the rejection with respect to the term "derived". In addition, Applicant's representative explained that the phrase "functional deletions" should not be amended to simply "deletions" because functional deletions can include deletions, as well as insertions, substitutions, or other mutations that decrease the function of such sequences. Applicant's representative agreed to clarify where in the application the phrase "functional deletion" is defined. Lastly, Applicant's representative agreed to clarify the phrase "substantially eliminate" to a particular percentage decrease in packaging, as supported by the specification.

With regard to the 35 U.S.C. § 112, second paragraph rejection of claim 15, it was agreed that inserting language to clarify that syncytia formation is decreased relative to a wild-type HIV-2 vector would overcome the rejection.

With regard to the 35 U.S.C. § 112, second paragraph rejection of claim 17, Applicant's representative agreed to clarify the claim.

With regard to the 35 U.S.C. § 112, second paragraph rejection of claims 21 and 43, it was agreed that inserting the term "isolated" would overcome the rejection.

With regard to the 35 U.S.C. § 112, first paragraph rejections, it was agreed that a Rule 132 Declaration signed by an expert in the art stating that it would be straight-forward to delete a few nucleotides from the upstream or downstream packaging signal sequences, would overcome the rejection.

With regard to the 35 U.S.C. § 103(a) rejection, it was agreed that a Rule 131 Declaration signed by the inventor swearing behind the date of publication of the Poeschla *et al.* (*J. Virol.* 72:6527-36, 1998) article would eliminate the document as prior art, thereby making the rejection moot.

Specification Amendments

The specification has been amended to note that the parent application has issued as US Patent No. 6,790,657, as requested by the examiner, and to remove references to hyperlinks.

Claim amendments

Claim 7 was amended to clarify the claim. Support can be found on throughout the application, for example on page 33, lines 10-12 and FIG. 8.

Claim 12 was amended due to the cancellation of claim 10.

Claim 15 was amended to correct an obvious typographical error and to clarify the claim. Support can be found throughout the application, for example on page 33, line 21 – page 35, line 3, as well as FIG. 10.

Claim 17 was amended to clarify the claim. Support can be found throughout the application. For example, support for the phrase "HIV-2 virions that contain vector RNA but not native viral RNA" can be found on page 11, lines 15-30 and on page 20, lines 14-15, and support for the phrase "leader sequence upstream from a" can be found on page 4, line 10.

Claims 21 and 43 were amended to clarify that the cell is an isolated cell. Support can be found throughout the application, for example on page 60, lines 10-11.

Support for the new claims can be found throughout the application, for example:

Claim 47: page 4, line 35, and page 26, lines 34-36 (SED ID NO: 4 is the nucleic acid sequence of the pROD(SD36) vector).

Claims 48-49: page 5, lines 1-5; page 11, lines 31-37; page 21, lines 12-16; page 27, lines 3-10; page 42, line 10 – page 43, line 6; and FIGS. 4A-4E.

Claim 50: original claim 7 and page 9, line 34

Claims 51-59: page 5, lines 11-12; page 11, lines 23-37; page 12, lines 1-3; page 20, line 9; page 27, lines 11-14; Example 18 (starting on page 57), and FIGS. 5A-5C.

Claim 53: FIG. 5B.

No new matter is introduced by these amendments. In addition, no amendments were made to distinguish prior art.

Claim objections

Claim 15 has been amended to correct the spelling of the word "syncytia" as requested by the examiner.

Claim 10 has been cancelled.

35 U.S.C. § 112, second paragraph

Claims 7-15, 17, 21 and 43-46 were rejected under 35 U.S.C. § 112, second paragraph as indefinite.

Claim 7 has been amended to remove the redundant "derived" language. In addition, the phrase "substantially eliminate" has been amended to "reduce packaging of progeny viral RNA by more than 80%" for clarification. The phrase "functional deletions" was not changed, as functional deletions can include deletions, as well as insertions, substitutions, or other mutations. The phrase "functional deletion" is defined in the application on page 9, lines 33-35.

Claim 15 has been amended to clarify that syncytia formation is decreased relative to an HIV-2 vector that has functional upstream and downstream packaging signal sequences.

Claim 17 has been amended to clarify that the HIV-2 virion can package vector RNA, but not its own RNA.

Claims 21 and 43 have been amended to clarify that the cell is an isolated cell.

In view of these amendments and explanations, Applicant requests that the 35 U.S.C. § 112, second paragraph rejections be withdrawn.

35 U.S.C. § 112, first paragraph

Claims 7, 8, 10, 14, 15, and 43 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. In addition, Claims 7, 8, 11, 14, 15, 17, 21 and 43 were rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. Applicant respectfully disagrees and requests reconsideration.

Applicant has provided several examples of packaging vectors, including HIV-2 and SIV packaging vectors. For example, three different HIV-2 packaging vectors derived from pROD with deletions upstream and downstream of the splice donor site are disclosed in SEQ ID NOS: 4-6 (also see FIGS 3C-3E). Based on the known sequence of SIV, the corresponding SIV packaging vectors can be made. For example, the SIV sequence that corresponds to the HIV-2 packaging vector SD36 (SEQ ID NO: 4) is shown in FIG. 5B (SEQ ID NO: 11). In addition, packaging vectors that have alternative promoters, such as a CMV promoter are provided (for example see SEQ ID NOS: 22 and 23). Furthermore, that the packaging vectors can be divided into two separate vectors is disclosed (for example see Example 6 on page 43). Particular examples are shown in SEQ ID NOS: 11, 21, 22, and 23. Therefore, Applicant has disclosed many examples of the claimed genus, and has therefore provided written description and enablement of the genus.

Methods for making any number of mutations to an HIV-2 or SIV vector are known. In addition, the application provides support for testing such mutations. For example, Example 4 on page 37 of the application describes methods that can be used to identify those sequences upstream and downstream of the SD that are necessary and sufficient for packaging.

It is routine to make different lengths of deletions in upstream and downstream packaging sequences. For example, it is straight-forward for those skilled in the art to make even a few nucleotide changes (such as single, double, triple, or greater numbers of nucleotides) to a lentivirus vector sequence, and test the resulting vector's ability to decrease packaging of native viral RNA using the methods disclosed in the application (for example see page 32, starting at

line 24). As stated in paragraph 4 of the enclosed Rule 132 Declaration of Dr. Kafri (an expert in the field of lentivirus vectors for gene therapy, recombinant nucleic acid methods can be used to generate deletions (or other alterations) within upstream and downstream packaging sequences.

It would not require undue experimentation to determine what range of mutations can be made to upstream and downstream packaging sequences to achieve a functional deletion that decreases packaging of progeny viral RNA. As noted above, introducing mutations into a lentiviral vector sequence, such as the upstream and downstream packaging sequences, is routine in the art. By making progressive deletions using recombinant nucleic acid methods, and determining which of these have decreased packaging of viral RNA using routine methods, one skilled in the art can identify the range of mutations can be made to upstream and downstream packaging sequences to achieve a functional deletion that decreases packaging of progeny viral RNA. As stated in paragraph 5 of the enclosed Rule 132 Declaration of Dr. Kafri, progressive deletions permit the identification of the minimal deletion needed in the upstream and downstream packaging signal to achieve an HIV packaging defective vector.

Therefore, Applicant requests that the 35 U.S.C. § 112, first paragraph rejections be withdrawn.

35 U.S.C. § 103(a)

Claims 7-15, 17, 21, and 43-46 were rejected under 35 U.S.C. §103(a) as obvious in view of Poeschla *et al.* (*J. Virol.* 72:6527-36, 1998) and MacCann *et al.* (*J. Virol.* 71:4133-7, 1997). Applicant respectfully disagrees and requests reconsideration.

Enclosed is a Rule 131 Declaration signed by inventor Dr. Arya, stating that he was in possession of the invention prior to the publication date of Poeschla *et al.* (*J. Virol.* 72:6527-36, 1998). Poeschla *et al.* was published in August 1998, while Dr. Arya's publication disclosing packaging vectors was published about two months earlier in June 1998. Therefore, Poeschla *et al.* is not available as prior art against the present application.

In view of this Declaration, and the unavailability of Poeschla *et al.* as prior art against the present application, Applicant requests that the 35 U.S.C. §103(a) rejection be withdrawn.

If there are any minor issues to be resolved before a Notice of Allowance is granted, the examiner is invited to telephone the undersigned.

Respectfully submitted,

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